

WE CLAIM:

1. A process for modifying a cyclic peptide ring nucleus comprising the steps of:

- (i) providing a cyclic peptide compound comprising a peptide unit having a γ -hydroxyl group;
- (ii) opening the ring of said cyclic peptide compound to provide a first linear peptide wherein said peptide unit having a γ -hydroxyl group is the N-terminus peptide unit of said first linear peptide;
- (iii) cleaving-off said peptide unit having a γ -hydroxyl group to provide a second linear peptide;
- (iv) attaching at least one amino acid, dipeptide unit or synthetic unit to said second linear peptide to produce a third linear peptide;
- (v) cyclizing said third linear peptide to produce a modified cyclic peptide compound having a modified ring nucleus.

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2. The process of Claim 1 wherein said amino acid, said dipeptide unit or said synthetic unit of step (iv) comprises a protected amino group.

3. The process of Claim 2 further comprising

- (vi) deprotecting said protected amino group to provide a deprotected amino group;
- (vii) acylating said deprotected amino group.

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4. The process of Claim 1 or Claim 2 further comprising cleaving another peptide unit from said second linear peptide in step (iii) before attaching said at least one amino acid, dipeptide unit or synthetic unit in step (iv).

5. The process of Claim 1 wherein step (iii) is performed by adding trifluoroacetic acid or hydrochloric acid to said first linear peptide in an organic solvent.

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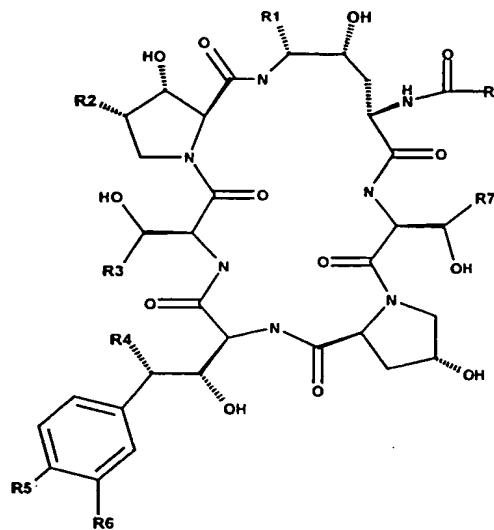
6. The process of Claim 5 wherein said organic solvent is selected from the group consisting of methylene chloride, toluene and dioxane.

10 7. The process of Claim 1 or 2 wherein a second amino acid, dipeptide or synthetic unit is attached to said third linear peptide in step (iv) prior to cyclizing in step (v).

15 8. The process of Claim 4 wherein a second amino acid, dipeptide or synthetic unit is attached to said third linear peptide in step (iv) prior to cyclizing in step (v).

9. The process of Claim 1 wherein said cyclic peptide compound is a cyclic hexapeptide.

20 10. The process of Claim 1 wherein said cyclic peptide compound is represented by the following structure:

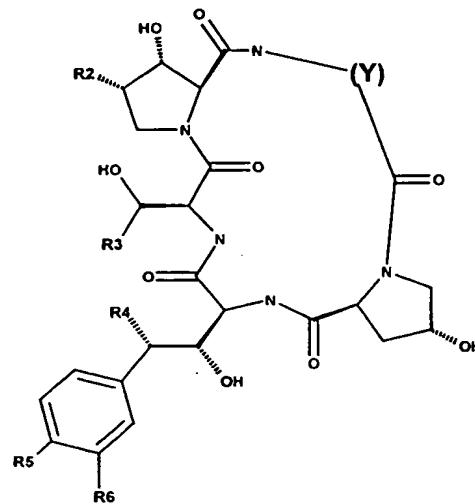


wherein R is an alkyl group, an alkenyl group, an alkynyl group, an aryl group, or heteroaryl group; R¹ is -H or -OH; R² is -H or -CH₃; R³ is -H, -CH₃, -CH₂CONH₂ or -CH₂CH₂NH₂;

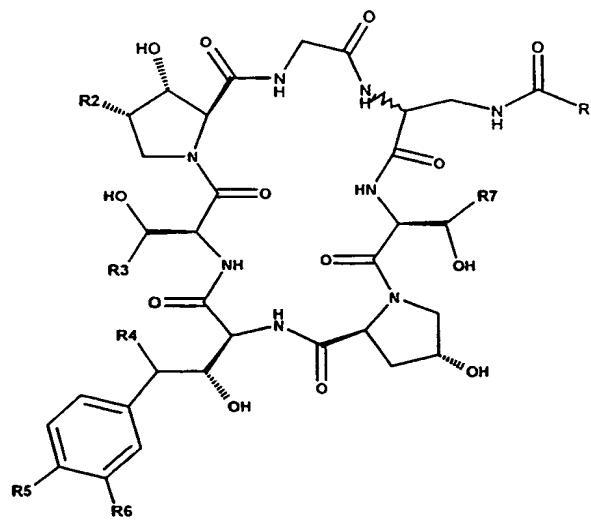
5 R⁴ is -H or -OH; R⁵ is -OH, -OPO₃H₂, or -OSO₃H; and R⁶ is -H or -OSO₃H.

11. The process of Claim 1 wherein said modified cyclic peptide compound is a 19-, 20-, 21-, or 22-membered ring compound.

10 12. A compound prepared by the process according to Claim 10 and represented by formula I or II:



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II

wherein

R is an alkyl group, an alkenyl group, an alkynyl group, an aryl group, or a heteroaryl group;

R^2 is -H or -CH₃;

R^3 is $=H$ $=CH_3$ $=O$

R^4 is -H or -OH:

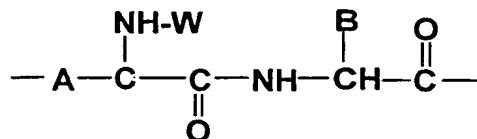
R^5 is $-\text{OH}$, $-\text{OPO}_3\text{H}_2$, or $-\text{OSO}_3\text{H}$;

R^6 is $-\text{H}$ or $-\text{OSO}_3\text{H}$;

R^7 is $-\text{CH}_3$ or $-\text{H}$;

(Y) is represented by the following formula

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wherein

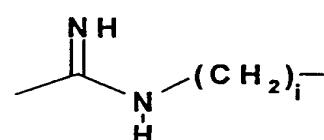
A is $-(\text{CH}_2)_a-$ where $a = 1-4$, $-\text{CHR}'-\text{CHR}''-(\text{CH}_2)_b-$ where R' and R'' are independently $-\text{H}$, $-\text{OH}$, $\text{C}_6\text{H}_5\text{O}-$, $-\text{SH}$,

10 $-\text{NH}_2$, $\text{C}_n\text{H}_{n+2}\text{NH}-$, $\text{C}_n\text{H}_{n+2}\text{O}-$, $\text{C}_n\text{H}_{n+2}\text{S}-$ or $-\text{C}_n\text{H}_{n+2}$ where $n = 1-4$ and $b = 0-1$, $-(\text{CH}_2)_c-\text{C}(\text{O})\text{NH}(\text{CH}_2)_d-$ where

$c = 1-2$ and $d = 1-2$, $-\text{N}=\text{CH}-(\text{CH}_2)_e-$ where $e = 0-2$, $-\text{NR}'''(\text{CH}_2)_f-$ where R''' is $-\text{H}$, $-\text{C}(\text{O})\text{CH}_2\text{NH}_2$,

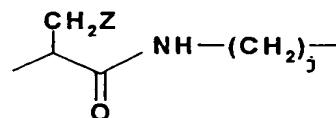
$-\text{C}(\text{O})\text{CH}(\text{NH}_2)\text{CH}_2\text{NH}_2$ or $-\text{C}_n\text{H}_{n+2}$ where $n = 1-4$ and

15 $f = 1-3$, $-(\text{CH}_2)_g-\text{SO}_2-(\text{CH}_2)_h-$ where $g = 1-2$ and $h = 1-2$,



where $i = 1$ or 2 , or

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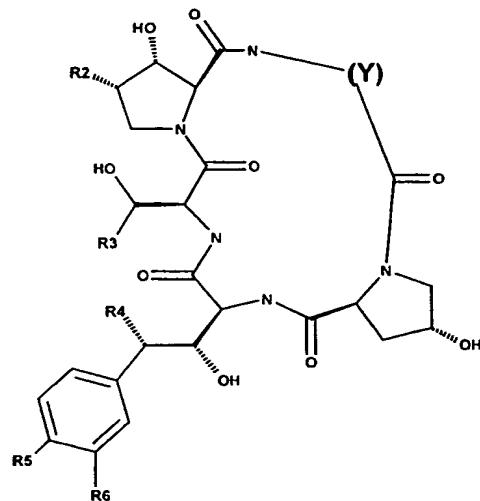
where j is 1 or 2 and Z is an amino group, alkylamino group, or piperidyl amino group; and

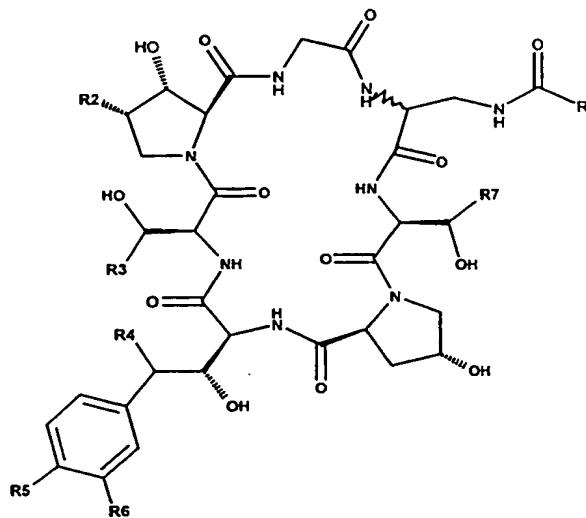
B is a substituted or unsubstituted C1 to C6 alkyl group;

W is a hydrogen or $C(O)R$ where R is as defined above;

5 and pharmaceutically acceptable salts, esters or hydrates thereof.

13. A compound represented by formula I or II:





III

5 wherein

R is an alkyl group, an alkenyl group, an alkynyl group, an aryl group, or a heteroaryl group;

R^2 is -H or -CH₃;

R^3 is -H, -CH₃, -CH₂CONH₂, or -CH₂CH₂NH₂;

R^4 is -H or -OH;

R^5 is $-\text{OH}$, $-\text{OPO}_3\text{H}_2$, or $-\text{OSO}_3\text{H}$:

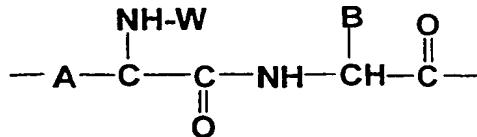
R⁶ is -H or -OSO₃H.

R^7 is $-CH_3$ or $-H$:

(Y) is represented by the following

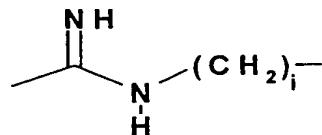
NH-W

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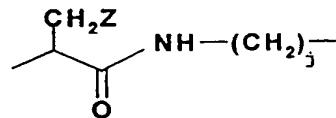
wherein

A is $-(CH_2)_a-$ where a = 1, 2 or 4, $-CHR'-CHR''-(CH_2)_b-$ where R' and R'' are independently -H, -OH, C_6H_5O- , -SH, -NH₂, $C_nH_{n+2}NH-$, $C_nH_{n+2}O-$, $C_nH_{n+2}S-$ or $-C_nH_{n+2}$ where n = 1-4 and b = 0, $-(CH_2)_c-C(O)NH(CH_2)_d-$ where c = 1-2 and d = 1-2, $-N=CH-(CH_2)_e-$ where e = 0-2, $-NR'''(CH_2)_f-$ where R''' is -H, $-C(O)CH_2NH_2$, $-C(O)CH(NH_2)CH_2NH_2$ or $-C_nH_{n+2}$ where n = 1-4 and f = 1-3, $-(CH_2)_g-SO_2-(CH_2)_h-$ where g = 1-2 and h = 1-2,



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where i = 1 or 2, or



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where j is 1 or 2 and Z is an amino group, alkylamino group, or piperidyl amino group; and

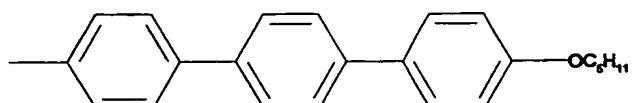
B is a substituted or unsubstituted C1 to C6 alkyl group;

W is a hydrogen or C(O)R where R is as defined above;

and pharmaceutically acceptable salts, esters or hydrates thereof.

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14. The compound of Claim 12 or 13 wherein R is a terphenyl group represented by the structure



15. A pharmaceutical composition comprising a compound of Claim 13 and a pharmaceutically inert carrier.

5 16. The pharmaceutical composition of Claim 15 further comprising a wetting agent, lubricating agent, emulsifier, suspending agent, preservative, sweetener, stabilizer, perfuming agent, flavoring agent or combinations thereof.

10 17. A method of inhibiting fungal activity comprising contacting a compound of Claim 13 with a fungus.

15 18. A method of treating a fungal infection in a human comprising administering to a human in need of such treatment a therapeutically effective amount of a compound according to Claim 13.

19. The method of Claim 18 wherein said compound is administered to said human topically, orally, by injection, by inhalation, or combinations thereof.

20 20. A method of inhibiting parasitic activity comprising contacting a compound of Claim 13 with a parasite.